

Novel intervention strategies for schistosomiasis elimination in Zanzibar

Submission date 21/01/2020	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 11/02/2020	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 28/11/2024	Condition category Infections and Infestations	<input type="checkbox"/> Individual participant data

Plain English Summary

Background and study aims

Urogenital schistosomiasis is a parasitic disease caused by flatworms such as *Schistosoma haematobium* that are released by freshwater snails. In line with the goals set by the World Health Organization for 2020 and 2030, the Zanzibar government is committed to eliminate urogenital schistosomiasis as a public health problem and to interrupt *Schistosoma haematobium* transmission from Zanzibar in the next years. Intensified mass drug administration (MDA) with biannual community-wide and school-based treatments started in 2012, and was complemented with additional interventions (snail control and behaviour change) within a trial conducted from 2012 to 2017. During this trial, several challenges on the last mile towards schistosomiasis elimination were identified. This study will address some of the identified challenges, including persistent hotspots of transmission, recurrence of infection, and diagnostics, and investigate new tools and strategies for breaking schistosomiasis transmission. The main aim of the study is to test the sensitivity of an adaptive surveillance-response system for its ability to detect *S. haematobium* infected individuals in low-risk areas to trigger an appropriate intervention response to avoid recurrence of infection.

The other aims are to reveal the performance of the surveillance-response system in terms of overall feasibility, timeliness, and acceptability. Moreover, the impact of intervention packages in hotspots and low-risk areas will be measured, the treatment coverage of (focal) MDA or test-and-treat in infected and healthy individuals will be assessed, and the performance of the diagnostic approaches used will be assessed.

Who can participate?

The study will be implemented in the North of Pemba island for 3.5 years. A cross-sectional baseline and three annual follow-up surveys will be conducted in schools and communities from 2020 to 2023. Schoolchildren, male and female, from nursery till grade 7 will be invited to participate in the school-based surveys. Participants of all sexes aged 4 years and older will be eligible to participate in the community-based surveys. Moreover, all community members aged 4 years and older will be eligible to be tested for *S. haematobium* infection during the surveillance activities implemented throughout the study years in low-risk shehias.

What does the study involve?

Participants will be tested for *S. haematobium* infection and blood in their urine. Participants will

be invited to answer a questionnaire about their past anti-schistosomal treatments and behaviours that might put them on risk for infection. Based on the *S. haematobium* infection prevalence determined in the annual cross-sectional surveys, study areas will be stratified in hotspots and low-risk areas. Hotspots will receive a combination of periodic MDA, snail control and behavior change interventions. Low-risk areas will receive targeted surveillance-response interventions, consisting of test-and-treat of high-risk groups, snail control in water bodies used by infected individuals, and health education of infected individuals.

What are the possible benefits and risks of participating?

The direct benefit from participation in the study is that participants will be informed about their *S. haematobium* infection status and will receive treatment with praziquantel if positive. The treatment can improve the general health status, including less pain, fatigue and weakness and thus improved school or working performance. Moreover, participating schools and shehia communities will benefit from the behaviour change interventions, including the implementation of laundry platforms and improved education about schistosomiasis prevention and transmission. Participating shehia communities will also benefit from snail control, which reduces the risk of *S. haematobium* transmission in the natural open water bodies of the targeted shehias.

For the participants, no risks are involved in producing a fresh urine sample. The questionnaires will include some questions that might be embarrassing, discomforting or too personal; however, participants can deny responding to these questions when they decide to participate.

Where is the study run from?

Swiss Tropical and Public Health Institute, Basel, Switzerland and Public Health Laboratory-Ivo de Carneri, Pemba, Tanzania

When is the study starting and how long is it expected to run for?

September 2019 to June 2024

Who is funding the study?

Swiss National Science Foundation (Switzerland)

Who is the main contact?

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Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

21.01.2020 (Version 2.1)

Study information

Scientific Title

The last mile: novel tools and strategies for breaking schistosomiasis transmission

Acronym

Schistobreak

Study hypothesis

The study does not test a null hypothesis because the primary analysis will estimate a population parameter. The parameter of interest is the sensitivity of the risk-based surveillance system.

The sensitivity (and corresponding confidence intervals) is estimated as:

$SE = \text{number of infected persons detected by the surveillance system} / \text{total number of infected persons}$

whereby the total number of infected persons is calculated from the cross-sectional surveys as:

$N_{inf} = \text{Prevalence}_{school} * N_{pop-school} + \text{Prevalence}_{non-school} * N_{pop-non-school}$

Ethics approval required

Old ethics approval format

Ethics approval(s)

1. Approved 23/10/2019, Ethics Committee Northwest and Central Switzerland (EKNZ) (Hebelstrasse 53, 4056 Basel, Switzerland; Tel:+41 (0)61 2681350; Email: eknz@bs.ch), ref: Project-ID: Req-2019-00951

2. Approved 13/12/2019, Zanzibar Health Research Ethical Committee (ZAHREC) (Ministry of Health Zanzibar, PO Box 236, Vuga Zanzibar; Tel: +255 (0)772 605560; Email: info@zahri.org), ref: NO.ZAHREC/03/PR/DEC/2019/12

Study design

Interventional surveillance study complemented by repeated cross-sectional surveys

Primary study design

Interventional

Secondary study design

Non randomised study

Study setting(s)

Community, School

Study type(s)

Other

Participant information sheet

Not available in web format, please use contact details to request a participant information sheet

Condition

Schistosoma haematobium infection

Interventions

The *S. haematobium* prevalence will be determined annually in cross-sectional surveys conducted in schools and communities of the study area. The baseline survey will be conducted in 2020, and follow-up surveys in 2021, 2022, and 2023. Depending on the *S. haematobium* prevalence, the study areas (shehias) will be stratified into hotspot or low-risk shehias and receive interventions accordingly for the year following the cross-sectional survey.

Inhabitants of hotspot shehias will receive mass drug administration (MDA) with praziquantel (40 mg/kg) as part of the routine interventions of the Neglected Tropical Diseases (NTD) Programme of the Zanzibar Ministry of Health (MoH) distributing praziquantel at least annually to the whole population of Zanzibar. Moreover, snail control using the molluscicide niclosamide will be carried out regularly in all natural waterbodies containing the intermediate host snails throughout the study years with the exception of the rainy season. Snail control will be carried out by experienced and trained research teams. Finally, behaviour change interventions containing interactive education in schools and communities using a pretested toolkit and safe laundry platforms will be implemented throughout the study years. Behaviour change activities will be carried out by experienced and trained research teams.

Inhabitants of low-risk shehias will not receive MDA. Here surveillance-response interventions will be carried out throughout the study years. Surveillance of high-risk groups will be done by a test-and-treat approach. Individuals infected with *S. haematobium* will receive a single dose of praziquantel (40 mg/kg) by staff of the research teams in collaboration with the Zanzibar NTD Programme. Additional response interventions will include snail control in infested water bodies of low-risk shehias and education of infected individuals on how to prevent *S. haematobium* transmission and infection.

Intervention Type

Mixed

Primary outcome measure

The number of *S. haematobium* infected individuals detected and reported through the surveillance system divided by the number of positive individuals in the population as extrapolated from the cross-sectional surveys, i.e. the mean sensitivity of the surveillance-response system determined over 3 years. *S. haematobium* infections will be determined by the

urine filtration method (detecting *S. haematobium* eggs in 10 ml urine) and reagent strip method (Hemastix; detecting microhaematuria in urine) applied on a single urine per participant in annual cross-sectional surveys (i.e. at baseline in 2020 and follow-up surveys in 2021, 2022, and 2023). For surveillance of high-risk groups the researchers will use the reagent strip method as a rapid test indicator for *S. haematobium* infections throughout the study years (2020 till 2023).

Secondary outcome measures

1. Performance parameters of the surveillance system:

1.1. Sensitivity of surveillance-response system for each study year (*S. haematobium* infection measured by the urine filtration method, by reagent strips and new rapid diagnostic tests once available; determined throughout the years during surveillance and in annual cross-sectional surveys in 2020, 2021, 2022 and 2023)

1.2. Timeliness of case notification and reactive intervention throughout the study years (time from case notification by active and passive surveillance to reactive intervention; measured by comparing the dates of records pertaining to surveillance and response throughout the study years 2020 till 2023)

1.3. Acceptability of surveillance-response throughout the study years (feedback from study participants with regard to surveillance-response activities; annually measured by questionnaire interviews during cross-sectional surveys interviews in 2020, 2021, 2022 and 2023)

2. Impact of interventions in hotspots over time:

2.1. *S. haematobium* prevalence in annual cross-sectional surveys (*S. haematobium* egg absence/presence in 10 ml urine measured by urine filtration and microhaematuria absence/presence measured by reagent strips; annually measured during cross-sectional surveys in 2020, 2021, 2022 and 2023)

2.2. *S. haematobium* infection intensity in annual cross-sectional surveys (*S. haematobium* egg counts in 10 ml urine; measured by urine filtration; annually measured during cross-sectional surveys in 2020, 2021, 2022 and 2023)

3. Impact of reactive interventions in low-risk areas over time:

3.1. *S. haematobium* prevalence in annual cross-sectional surveys (*S. haematobium* egg absence/presence in 10 ml urine measured by urine filtration and microhaematuria absence/presence measured by reagent strips; annually measured during cross-sectional surveys in 2020, 2021, 2022 and 2023)

3.2. *S. haematobium* infection intensity in annual cross-sectional surveys (*S. haematobium* egg counts in 10 ml urine; measured by urine filtration; annually measured during cross-sectional surveys in 2020, 2021, 2022 and 2023)

4. Treatment coverage of MDA or test-and-treat in infected and healthy individuals:

4.1. Coverage and compliance with praziquantel treatment in the round of MDA preceding the cross-sectional survey in hotspot areas, determined in annual cross-sectional surveys (coverage = receiving praziquantel tablets during MDA, compliance = swallowing praziquantel tablets in the dose supplied during MDA; annually measured during cross-sectional surveys in 2020, 2021, 2022 and 2023)

4.2. Percentage of total shehia population treated by risk-based test-and-treat in low-risk areas throughout the study years (measured by records of test-and-treat activities throughout the study years 2020 till 2023)

5. Performance of diagnostic approaches:

5.1. Diagnostic sensitivity (percentage of true *S. haematobium* positive individuals, correctly diagnosed by the test under investigation in comparison with a reference test)

5.2. Diagnostic specificity (percentage of true *S. haematobium* negative individuals, correctly diagnosed by the test under investigation in comparison with a reference test)

Overall study start date

01/09/2019

Overall study end date

30/06/2024

Eligibility

Participant inclusion criteria

1. All persons aged >3 years, living in the study shehias
2. Submitted informed consent form (ICF) signed by parent or legal guardian in case of participating children and adolescents, or signed by the participant in case of participating adults
3. One urine sample with sufficient volume to perform diagnostic tests provided

Participant type(s)

All

Age group

Mixed

Lower age limit

3 Years

Sex

Both

Target number of participants

This is an implementation research study with the goal to test an adaptive intervention strategy that contributes towards the interruption of *S. haematobium* transmission. For surveillance, the researchers will annually test 10,000 individuals (ca. 33% of the population in 10 shehias). Hence, in three study years, they will test a total of 30,000 individuals. In cross-sectional surveys, they will annually test 6,970 individuals (ca. 10% of the population in the 17 shehias). Hence, in four surveys, they will test a total of 27,880 individuals .

Participant exclusion criteria

1. Children ≤ 3 years
2. Children, adolescents and adults not living in the study area
3. ICF not submitted or not signed by parent or legal guardian in case of participating children or adolescents or not signed by the participant in case of participating adults
4. No urine sample of sufficient volume to perform diagnostic tests provided

Recruitment start date

15/05/2020

Recruitment end date

30/06/2024

Locations

Countries of recruitment

Tanzania

Study participating centre

Public Health Laboratory – Ivo de Carneri (PHL-IdC)

PO Box 122, Wawi

Chakechake

Tanzania

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Sponsor information

Organisation

Swiss Tropical and Public Health Institute

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Sponsor type

Research organisation

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Funder(s)

Funder type

Research organisation

Funder Name

Schweizerischer Nationalfonds zur Förderung der Wissenschaftlichen Forschung

Alternative Name(s)

Schweizerischer Nationalfonds, Swiss National Science Foundation, Fonds National Suisse de la Recherche Scientifique, Fondo Nazionale Svizzero per la Ricerca Scientifica, Fonds National Suisse, Fondo Nazionale Svizzero, Schweizerische Nationalfonds, SNF, SNSF, FNS

Funding Body Type

Private sector organisation

Funding Body Subtype

Trusts, charities, foundations (both public and private)

Location

Switzerland

Results and Publications

Publication and dissemination plan

The researchers plan to publish the study protocol in the peer-reviewed literature in 2020. They intend to publish their study results in the peer-reviewed (whenever possible open-access) literature and international conferences by mid 2024.

Intention to publish date

30/08/2025

Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other publications	Evaluation of tablet-based fine-scale mapping approach	15/01/2022	17/01/2022	Yes	No
Other publications	Baseline parasite infection prevalence and intermediate host abundance	16/08/2022	30/08/2022	Yes	No
Protocol article		30/09/2021	30/08/2022	Yes	No
Results article		02/07/2024	03/07/2024	Yes	No
Other publications		13/11/2024	20/11/2024	Yes	No
Other publications		26/11/2024	28/11/2024	Yes	No